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Synthetic musk compounds as MXR inhibitors

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Abbreviations

FSW: filtered seawater, K_{ow}: octanol-water coefficient, MXR: Multixenobiotic resistance, PPCPs: pharmaceutical and personal care products, MK: musk ketone, MX: musk xylene, for abbreviations of other compounds see Table 1

Section headers

Abstract

Synthetic musk compounds, widely used as fragrances in consumer products, have been detected in human tissue and, surprisingly, in aquatic organisms such as fish and mollusks. Although their persistence and potential to bio-accumulate are of concern, the toxicity and environmental risks of these chemicals are generally regarded as low. Here, however, we show that nitromusks and polycyclic musks inhibit the activity of multi-drug efflux transporters responsible for multi-xenobiotic resistance (MXR) in gills of the marine mussel *Mytilus californianus*. The IC10 values for the different classes of musks were in the range from 0.09 to 0.39 μM and IC50 values were between 0.74 and 2.56 μM. The immediate consequence of inhibition of efflux transporters is that normally excluded xenobiotics will now be able to enter the cell. Remarkably, the inhibitory effects of a brief two-hour exposure to musks were only partially reversed after a 24 to 48-hour recovery period in clean seawater. This unexpected consequence of synthetic musks — a long-term loss of efflux transport activity — will result in continued accumulation of normally excluded toxicants even after direct exposure to the musk has ended. These findings additionally point to the need to determine whether other environmental chemicals have similar long-term effects on these transporters. The results are relevant to human health, as they raise the possibility that exposure to common xenobiotics and pharmaceuticals could cause similar long-term inhibition of these transporters and lead to increased exposure to normally excluded toxicants.